Update in Community-Acquired Pneumonia

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Roadmap

• Background
• Etiology
• Diagnosis
• Treatment
• Prevention

Specific Goals:

• Describe the most common causes of community-acquired pneumonia in the outpatient setting
• Order appropriate diagnostic tests for CAP
• Initiate appropriate antibiotics in the treatment of community-acquired pneumonia (CAP)
• State the optimal duration of therapy in CAP
• State the benefits and need for preventative measures for CAP
Caveats

- Will not talk about healthcare-associated pneumonia (HCAP)
- Will not discuss admission decision (complex)
- Syllabus (sharpeb@medicine.ucsf.edu)

CAP: Background

- 5 million cases/year in the U.S.
- 80% of CAP is treated outpatient
- Sixth leading cause of death
- Inpatient mortality 10-35%
- Outpatient mortality < 1%

CAP: Background

- Higher mortality among Caucasians
- Some evidence that quality of care for African-Americans with CAP is worse

Cough 90%*
Dyspnea 66%
Sputum 66%
Pleuritic chest pain 50%

* Yet, only 4% of all visits for cough are pneumonia

Clinical Presentation: Geriatrics

- Less “classic” presentations
  - 10% have NONE of the classic signs or symptoms
- Up to 40% will not have fever
- Up to 45% will have altered mental status

“Typical” vs. “Atypical”

- Classic teaching is not supported by the literature
- Some general trends
  - S. pneumoniae in older pts, co-morbidities
  - Viruses more common in older patients
  - Mycoplasma in patients < 50 years old

“Typical” vs. “Atypical”

- Classic teaching is not supported by the literature
- Some general trends
  - But - no history, exam, laboratory, or radiographic features predict organism
    - “Walking pneumonia”
    - “Classic lobar pneumonia”

Microbiology of CAP

- Prospective study of 2320 patients with CAP admitted to 5 hospitals
- All extensive diagnostic evaluation
  - Blood cultures, sputum cultures
  - Urine antigen for S. pneumoniae & Legionella
  - Nasopharyngeal PCR for viruses, Chlamydophila, Mycoplasma
  - Some serologic testing

Jain S, et al. NEJM
Microbiology of CAP

1) Rhinovirus
2) Influenza
3) Streptococcus pneumoniae

Jain S, et al. NEJM. 2015

Microbiology of CAP

- Real-time PCR was applied to sputum samples from 323 patients with CAP
- Pathogen confirmed in 87% of patients
  - H. Flu and Strep pneumo most common
  - Viruses in 30% but > 80% co-infections


Etiology of CAP

Outpatients (mild)
- Resp. viruses
- S pneumoniae
- M pneumoniae
- C pneumoniae
- H influenzae

Non-ICU inpatients
- Resp. viruses
- S pneumoniae
- M pneumoniae
- C pneumoniae
- H influenzae
  - Legionella spp

ICU inpatient
- S pneumoniae
- Legionella
- H influenzae
- GNRS
- S aureus
- Resp. viruses (?)

Metlay JP, et al. JAMA 1997;276(17):1440

Take Home Points

1) 
2) 
3) 
4) 
5)
**Diagnosis of CAP**

1) Select clinical features  
(e.g. cough, fever, sputum, pleuritic chest pain)

AND

2) Infiltrate by CXR or other imaging

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**Chest Radiograph – Gold Standard**

- All expert guidelines state should have positive CXR to make diagnosis
  - History, exam, etc. not good enough
- In outpt setting, should see an infiltrate.  
  - Order CXR if you are concerned about CAP  
  - If CXR negative, likely should not treat for CAP
- In the inpatient setting, the CXR can be negative

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**Chest Radiograph – Gold Standard?**

- Should order CXR in all patients with suspected pneumonia.
- In the hospital, a positive CXR is not necessary to treat as CAP (but consider other diagnoses).

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**Blood Cultures**

- Specific organism vs. contaminants, cost
- Reality:
  - No evidence of a benefit
  - Rarely positive = _____
  - Contaminant rate = _____
  - More likely to be positive if sicker
    - ICU, septic shock, etc.
**Blood Cultures in CAP**

- In general, do not get blood cultures for outpatient CAP
- For inpatient CAP, blood cultures are **optional**
- Consider if risk factors:
  - ICU, severe sepsis, cavitary infiltrates, pleural effusion

**Sputum for CAP**

- Complicated and controversial
- Simple, inexpensive, specific for pneumococcus
- Problems include:
  - Up to 30% could not produce adequate sputum
  - Good quality available in only 14%
  - Most don’t narrow antibiotics

**Sputum Cultures in CAP**

- In general, sputum cultures are **not** indicated in outpatient CAP
- For inpatient CAP, sputum is indicated:
  - High-quality specimen, right to the lab
  - ICU, cavitary infiltrates, underlying lung disease

**The future in CAP - biomarkers**

- Procalcitonin: precursor of calcitonin
  - No hormonal activity
  - Inflammatory marker
  - Increased in sepsis, bacterial infection
**Meta-analysis/systematic review**

- Four studies, ~3500 patients with respiratory tract infections
- Less antibiotic exposure**
  - A 22% decrease in prescriptions
  - Average 2.3 days less abx overall
- No difference in mortality/clinical outcomes


**Take Home Points**

1) Cover typical and atypical bacteria
2)
3)
4)
5)

**Roadmap**

- Background
- Etiology
- Diagnosis
- **Treatment**
- Prevention

**Treatment Principle #1**

Outpatients (mild)

- Resp. viruses
- *S pneumoniae*
- *M pneumoniae*
- *C pneumoniae*
- *H influenzae*

Must cover all these organisms*

- Come back on Friday for a review of new data on atypical coverage
Treatment Principle #2

Outpatients (mild)

- Resp. viruses
- S pneumoniae
- M pneumoniae
- C pneumoniae
- H influenzae

"Wimpy" pneumococcus

Drug-resistant S. pneumoniae (DRSP)

Penicillin, erythromycin, macrolides, etc.

Risk Factors for DRSP

- Age > 65 years old
- Chronic disease
  - Heart, lung, renal, liver
- Diabetes mellitus
- Alcoholism
- Malignancy (active)
- Immunosuppression
- Antibiotics in the last 3 months

Treatment CAP

Outpatient, healthy, no DRSP risk factors

Doxycycline or macrolide

Macrolide = azithro, clarithro, erythro

Treatment CAP

Outpatient, DRSP risk factors

Oral fluoroquinolone
OR
Oral β-lactam + doxy or β-lactam + macrolide

- Oral fluoroquinolone: moxi, gimi, levofloxacin
- β-lactam: High-dose amoxicillin (1gm PO tid) Augmentin (875mg PO bid)
Take Home Points

1) Cover typical and atypical bacteria
2) Get the CXR, skip the cultures
3)
4)
5)

Treatment CAP

<table>
<thead>
<tr>
<th>Inpatient, non-ICU</th>
<th>Fluoroquinolone OR β-lactam + macrolide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient, ICU</td>
<td>IV β-lactam + macrolide + vancomycin OR</td>
</tr>
<tr>
<td></td>
<td>IV β-lactam + fluoroquinolone + vancomycin</td>
</tr>
</tbody>
</table>

Duration of therapy?

- Meta-analysis of 15 RCTs, 2796 patients with mild to moderate CAP
- Compared short-course (< 7 days) with longer courses.
- Looked at clinical failure, bacterial eradication, and mortality.

Duration of therapy?

- No difference in clinical failure
- No difference in bacterial eradication
- No difference in mortality

- In subgroup analysis, trend toward favorable efficacy with short-course.
Duration of therapy?

- RCT of 312 pts. admitted with CAP
- Randomized to 5 days vs. usual care
  - If afebrile x 48 hours
- No difference in cure rates or mortality


Duration of therapy

- Start at 5 days total
  - If afebrile x 48 hours and clinically well
  - Can extend at your discretion
  - Most will only need 7 days or less

Steroids in Pneumonia?

Take Home Points

1) Cover typical and atypical bacteria
2) Get the CXR, skip the cultures
3) Outpatient: Brad Pitt vs. Donald Rumsfeld
4) 
5)
Follow-up CXR?

- Standard practice?
- Prior ATS guidelines said yes, recent guidelines do not address
- CXR resolution:
  - At 28 days, ~ 50% had not resolved
- Can consider in “high-risk” patients
  - Significant smoking history, etc.
  - Probably should wait > 3 months

Bruns AH. CJD. 2007;45:983.

Pneumovax

- Updated meta-analysis of 18 RCTs (~64,000 pts) and 7 non-RCTs (~62,000 pts) trials,
- Only high-quality studies

<table>
<thead>
<tr>
<th>Relative Risk</th>
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<tbody>
<tr>
<td>All-cause pneumonia</td>
<td>0.70 (0.45-1.12)</td>
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<tr>
<td>All-cause mortality</td>
<td>0.90 (0.74-1.09)</td>
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** No difference for elderly or chronic illness


Pneumovax - Efficacy

- Four different trials looking at benefits of pneumovax in patients hospitalized with CAP.
- Compared vaccinated vs. non-vaccinated
- Looked at impact on ICU admission, inpatient mortality, inpatient complications, and LOS.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>ICU admission</td>
<td>Decreased</td>
</tr>
<tr>
<td>Inpt complications</td>
<td>Decreased</td>
</tr>
<tr>
<td>LOS</td>
<td>Decreased</td>
</tr>
<tr>
<td>Inpt mortality</td>
<td>Decreased</td>
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CAP: Current & Future
Pneumovax - Efficacy

- Pneumococcal vaccine likely prevents invasive pneumococcal disease.
- Probably reduces death, ICU admission, complications, and LOS in patients hospitalized with CAP (“makes pneumonia less bad”)

Influenza Vaccine - Efficacy

- Adults aged < 65 years
  - Prevents influenza illness in ~ 70-90%
- Adults aged > 65 years
  - Prevents influenza illness in ~ 30-70%

Proton Pump Inhibitors

  -- Current use of PPI: CAP OR = 1.5
  -- Recent start: CAP OR = 5.0
  -- Recent PPI start: CAP OR = 3.8
  -- 52% of hosp pts got PPI, HAP OR = 1.3
  -- Rates recurrent CAP after CAP admit
  -- Starting PPI: OR 2.1% (7% abs risk)

Hospitalization Risk Reduction

<table>
<thead>
<tr>
<th>Hospitalization</th>
<th>Risk Reduction</th>
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<tbody>
<tr>
<td>Hospitalization for pna/flu</td>
<td>27%*</td>
</tr>
<tr>
<td>All cause death</td>
<td>48%*</td>
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* All p values < 0.001

### Anti-psychotics

  -- Recent anti-psychotic start (1 wk); OR 4.3**

  -- Population based study, 2000 patients.

<table>
<thead>
<tr>
<th>Current Use</th>
<th>Risk of pneumonia</th>
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<tbody>
<tr>
<td>Typical anti-psychotic</td>
<td>OR = 2.6 (1.4-4.6)</td>
</tr>
<tr>
<td>Atypical</td>
<td>OR = 1.8 (1.2-5.3)</td>
</tr>
</tbody>
</table>

### Take Home Points

1) Cover typical and atypical bacteria  
2) Get the CXR, skip the cultures  
3) Outpatient: Brad Pitt vs. Donald Rumsfeld  
4) Treat for 7 days  
5) Vaccines = good